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The Value of Ablation Parameter Indices for Predicting Mature Atrial Scar Formation in Humans: An *In Vivo* Assessment using Cardiac Magnetic Resonance Imaging

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Short Title

VisiTag and CMR-defined ablation scar

Relationships with industry

None declared

Abstract

Introduction:

The VisiTag module (CARTO3) provides an objective assessment of radiofrequency (RF) ablation parameters. This study aimed to determine the predictive value and optimal VisiTag threshold settings for prediction of gaps in mature atrial scar, as assessed non-invasively using cardiac magnetic resonance (CMR) imaging.

Methods:

24 subjects (11 paroxysmal AF) underwent first-time RF ablation with operators blinded to VisiTag data. 3D LGE CMR scans were performed at 3 months ($1.3x1.3x4mm^3$). A survey of UK operators defined standard VisiTag settings ('Force' 8g, 'Time' 10seconds, 'Percentage Time' 50%, 'Range' 3mm, 'Impedance' and 'Temperature' 'off'). Each ablation procedure was exported 27 times, varying single VisiTag parameters from default values. The presence of gaps in VisiTag markers (18 sectors) was assessed for each export and compared to gaps in CMR enhancement.

Results:

At default settings, VisiTag gaps were specific (97.5%) but less sensitive (50.4%) for CMR gaps. Sensitivity improved at higher thresholds (89.2% at 20g, 85.6% at 30sec, 88.5% Impedance 10Ω, 92.8% Temperature 42°C), but with lower positive predictive value (42.3%, 42.7%, 41.1% and 37.7% respectively, versus 90.9% at baseline). 'Force' thresholds demonstrated stable PPV from 2-8g ($p=0.24$), but a rapid fall at forces >10g. Binomial logistic regression model explained 41.7% of gaps ($\chi2(4)=148$, $p<0.0001$), correctly classifying 82% of cases (specificity 94.9%, sensitivity 56.8%).

Conclusion:

Gaps in VisiTags predict gaps in CMR LGE enhancement with high specificity at default settings. Sensitivity may be improved using more stringent thresholds, but at the potential cost of unnecessary ablation, particularly when a force >10g is stipulated.

Key Words

Atrial fibrillation, cardiac magnetic resonance imaging, structural remodeling, atrial fibrosis, catheter ablation

Introduction

Catheter-myocardial contact is a key determinant of ablation lesion formation, with many studies demonstrating the importance of contact force (CF) technology in the determination of ablation lesion quality and size (1–5) . Real-time CF measurement and display using CF-sensing catheters provides immediate feedback to the operator, improving catheter positioning (6) and estimation of radiofrequency (RF) energy delivery (3).

However, it has been recognized from the outset that absolute CF is only one of several factors contributing to RF lesion formation (7). Using electroanatomic mapping (EAM) systems, multiple parameters can be assessed simultaneously, including ablation time, catheter stability, impedance drop, and catheter tip temperature. Simple summative indices such as force time integral (FTI) have been shown to be associated with lesion formation (8), but there has been a drive towards more objective markers for predicting tissue injury. VisiTag (Biosense Webster, Diamond Bar, CA, USA) is a software module within the CARTO3 EAM system that was introduced in 2014 to permit quantification and display of RF-induced injury. It enables operators to select the values of a specified selection of parameters (including minimum CF, time at location, stability indices, impedance drop and temperature) that must be met in order for a VisiTag marker to be placed at the ablation location. As such, it is an objective marker of ablation parameters that is highly dependent upon operator-assigned thresholds.

Ex-vivo (9) and pre-clinical work (10) has contributed to informed selection of VisiTag thresholds, but there remains a wide variation between clinical operators (11, 12). The marker is also ascribed a single location on the atrial shell, and operators must interpret the distribution of VisiTags in their assessment of the adequacy of contiguity of lesions. There is therefore a need for the quantification of predictive value of VisiTags for chronic atrial ablation lesion formation in the clinical setting.

CMR imaging is the only currently available modality for non-invasive ablation lesion assessment, using late gadolinium enhancement (LGE) as a reproducible marker of fibrosis secondary to tissue injury (13). It must be recognized that the precise relationship between raw signal intensity on the LGE CMR image and histologically validated atrial ablation scar remains under investigation, and it is highly likely that all nuances of scar formation and density cannot be detected using a single technique. However, animal and human studies have demonstrated a strong correlation between ablation lesions and LGE signal intensity, as assessed histologically (10, 14) and by voltage mapping (15, 16), and therefore the technique is increasingly being used as a marker of mature ablation scar formation.

This study aimed to identify the optimal threshold settings for VisiTag parameters during human atrial ablation to predict mature atrial ablation scar, as assessed using the robust surrogate marker of CMR LGE enhancement.

Methods

Study population

Between March 2014 and September 2015, patients with a pre-procedural baseline CMR scan undergoing first-time ablation for AF were approached to join the study. Inclusion criteria included an ablation performed using the SmartTouch ablation catheter (Biosense Webster) and that the VisiTag module was activated for the entire ablation procedure. Exclusion criteria were a contraindication to further CMR imaging or prior allergic reaction to contrast agent. 24 patients in total were recruited. Subjects provided written and informed consent and returned for CMR scan assessment of atrial scar at 3 months. Baseline demographics and comorbidities were documented at the initial scan. The study was performed at St Thomas' Hospital, London, UK and was approved by the UK Health Research Authority (NRES Committee for South London, reference 08/H0802/68).

Ablation procedure

Two operators performed all catheter ablation procedures under general anaesthesia using CARTO3 (Biosense Webster)) EAM system. For patients with a diagnosis of PAF and in sinus rhythm, a point-by-point wide area circumferential ablation (WACA) achieving pulmonary vein isolation (PVI) was performed using the SmartTouch catheter (Biosense Webster, 8Fr irrigated). Operators were blinded to VisiTag placement, with VisiTags not displayed during ablation, but real-time contact force measurements were displayed. Lesion sites were recorded manually. Target ablation parameters were >5g for at least 15 seconds per stable RF delivery location, performed in temperature-control mode using a dragging technique. Power was 30W throughout except on the posterior wall, where it was limited to 25W. Procedural endpoint was defined as PV isolation confirmed by entry block (and exit block if PV capture could be achieved). For patients presenting with PersAF, a WACA was performed followed by additional ablation (mitral line, roof line, inferior LA and complex fractionated electrogram ablation) as a step-wise ablation (17).

CMR imaging acquisition and image interrogation

CMR imaging was performed on a 1.5T MR-scanner (Ingenia, Philips Healthcare, Best, Netherlands). A 3D LGE acquisition (3D inversion recovery spoiled gradient echo (LGE)) was performed at 30min after gadolinium injection (acquired resolution 1.3x1.3x4mm^3) (18) and post-ablation atrial scar (PAAS) within the 3D LGE dataset was interrogated using a maximum intensity projection technique (3mm outside semi-automated segmentation, 1mm inside segmentation) (13). This created a LA shell with projected signal intensities, indicating scar location. PAAS was thresholded using a histologically-validated value of 3.3 standard deviations (SDs) above the blood pool (BP) mean (14). Further details of imaging and processing techniques are provided in the online supplement.

VisiTag parameter survey

A questionnaire regarding prevailing practice in the use of contact force settings was sent in September 2015 to 35 UK centres performing AF ablation. The full set of questions with potential responses is presented in the online supplement. The responses were used to determine median ranges for the default VisiTag parameter settings (see below).

VisiTag data export

Ablation data was exported retrospectively, with location-specific VisiTag status ascribed directly by the CARTO3 system for each export with differing parameter settings. The default settings were selected based upon the median values of the UK survey (see Online Supplement) and each export varied only a single parameter from default values. A total of 27 export datasets were created for each subject, with the number of settings exported for each parameter weighted according to the perceived importance of the parameter in the UK survey (Table 1). Figure 1 illustrates the change in VisiTag distribution for a single subject with variation of 'Force' threshold alone; further examples are presented in the online supplement.

Comparison of ablation and CMR shells

The CARTO3 export datasets were processed using custom written Matlab software (MathWorks, MA, USA). For each subject, the LA shell was remeshed to create isotropic surfaces, and the 27 sets of VisiTag locations extracted. A 7.5mm search radius was defined for each triangle of the LA shell, and the surface triangles were binarised to those associated with a VisiTag marker (VisiTag 'shadow'), and those that were not. The 7.5mm search radius was defined based upon anticipated maximum lesion radius of 4.5mm at 30W and 10g force (19, 20), with the addition of the default "Range" threshold of 3mm. Shells were also generated with interrogation distances of 2.5, 5, and 10mm in order to test the lesion radius assumption. At 2.5mm and 5mm interrogation distance there were gaps in >90% of segments at standard parameters, which was felt to be implausible given the acute electrical isolation of all veins at the end of the procedure. At 10mm, there were no gaps except at the most stringent of parameter settings.

In order to facilitate comparison between CMR and ablation data, the CMR shell was registered to the ablation shell using an iterative closest point technique, blinded to both ablation and MRI signal data (21). In order to exclude the possibility that native atrial scar may have been present at the site of VisTag gaps, the pre-ablation atrial shells were also reviewed at the same threshold of 3.3SD above BP mean. The average scar burden at this (relatively high) threshold was 1.5±1.4%, almost exclusively at the right upper pulmonary vein (respiratory navigator artefact) and the mitral valve annulus. Across the 24 subjects, there was no overlap of pre-ablation enhancement and gaps in VisiTag lesions at default settings.

Lesion continuity assessment

The presence of a gap in CMR LGE scar was assessed at each of 18 sectors for each patient shell. Eight sectors were defined circumferentially around each vein pair, with a ninth, inter-ostial sector also defined on each side. The presence of a gap in VisiTag 'shadow' was assessed in blinded fashion for each sector for the 27 parameter setting groups using Paraview (Kitware, New York, NY, USA). The ablation line was considered continuous in the absence of any gap >1mm, representing the absolute CMR resolution limit. Distances were measured as a straight line between closest points of lesion apposition, using the 'Ruler' tool in Paraview. For continuous VisiTag variables ('Force', 'Time', and 'Percentage Time'), "thresholds" were defined as the most stringent parameter setting at which no gap in VisiTag 'shadow' was observed within a sector. 'Range' is not an ordinal scale variable, and therefore could not be analysed using this method (see Online Supplement). Instead, the total number of 'Range' thresholds settings that demonstrated continuous VisiTag 'shadow' (maximum 6 settings) was used as a surrogate summative index.

Statistical methods

Normally distributed continuous variables are presented as mean ± SD, and median with interquartile range (IQR) for non-normal distribution or non-continuous ordinal data. Statistics were analysed using SPSS Statistics (Version 22, Armonk, NY). For assessment of VisiTag accuracy for prediction of gaps in ablation scar, the locations of CMR-derived chronic scar were taken as the 'gold standard' indication of chronic lesion formation. Sensitivity and specificity of VisiTag 'shadow' prediction of CMR gaps was assessed using standard methods (outlined in Table 2) and used to derive receiver operator characteristic (ROC) curves. Within-patient differences for binary thresholding (impedance on/off, temp on/off) were compared using Wilcoxon matched-pairs signed rank test, and the non-parametric Friedman test was used for multi-setting parameters (force, time, range, percentage time).

Results

24 subjects were included in the study (Table 3).

An example of the variation in VisiTag 'shadow' with changing thresholds is shown in Figure 2, and the results of the CMR gap assessment are shown in the upper row of Figure 3. Gaps in the thresholded CMR LGE scar were present in 33% of sectors in total, with significant regional variation ($p<0.001$). The inter-ostial sector was ablated on the right in 13 patients (54%- 7 of whom (53%) had CMR gaps), and on the left in 9 patients (37%- 2 of whom (22%) had CMR gaps).

The sectors in which the highest 'Force' VisiTag thresholds could be applied without gaps being demonstrated between VisiTags 'shadows' were generally within the right anterior and left posterior regions (middle row Figure 3). A slightly different pattern was observed for 'Time' thresholds, where the highest threshold was observed infero-anteriorly (lower row Figure 3). Median 'Percentage Time' was 80% in all sectors.

The upper chart in Figure 4 demonstrates the overall accuracy of the VisiTags for detection of CMR gaps at default settings. There were gaps in the continuous VisiTag 'shadow' in 78 sectors (18%) (note that operators were blinded to VisiTags during ablation), and when a VisiTag 'shadow' gap was present it was very rare for there to be continuous CMR scar (low false positive rate, 7 (1.5%) of sectors, PPV 0.907). However, the false negative rate (no gap in VisiTag 'shadow' but gap on CMR) was higher (74 (17%) of sectors, NPV 0.791).

Individual Parameters

The ROC curves (Figure 4) demonstrate a significant relationship ($p<0.0001$) between a gap in VisiTag 'shadow' and gap in CMR LGE for all four parameters.

'**Force':** The number of sectors with VisiTag 'shadow' gaps increased significantly with increased threshold (66 sectors (15%) at 2g, 293 (67%) at 20g, ($p<0.001$). The sensitivity and specificity were 0.504 and 0.975 respectively at 8g, 0.626 and 0.822 at 12g, and 0.892 and 0.385 at 20g. The positive predictive value (PPV) and negative predictive value (NPV) for prediction of CMR gaps are shown in Figure 5. The NPV improved steadily with increasing ‘Force’ threshold, but there is a discontinuity in the progression of PPV. PPV was static between 2g and 8g (0.909 and 0.907 respectively, $p=0.24$) then decreased rapidly to 0.539 at 14g ($P<0.0001$): any gaps in VisiTag ‘shadow’ when threshold was ≤8g were highly likely to be associated with a gap in CMR scar, but at higher VisiTag thresholds (≥12g) continuous CMR scar was often formed without continuous VisiTag ‘shadows’ having been achieved.

‘**Time’:** VisiTag ‘shadow’ gaps also increased significantly with increased threshold (61 sectors (14%) at 5sec, 279 (64%) at 30sec, $p<0.001$), but with a more linear response to changes in threshold (Figure 5, top right chart). Sensitivity and specificity were 0.410 and 0.985 at 5 seconds, and 0.856 and 0.418 respectively at 30 seconds.

‘Percentage Time’: The presence of gaps in VisiTag ‘shadows’ changed a smaller amount across the ‘Percentage Time’ settings (71 sectors (16%) at 30%, 104 (24%) at 80%, $p<0.001$): the AUC predominantly represents the sensitivity and specificity of the default VisiTag parameters.

‘Range’: The effect of alteration in the ‘Range’ threshold is more complex parameter and is not ordinal (see Supplementary Data). Perhaps counter-intuitively, regions of the atrium may be associated with a VisiTag at smaller (more stringent) range settings, but not at larger (more lenient) ranges when ablation energy is ascribed to a more distant location. 119 sectors (27%) had VisiTag ‘shadow’ gaps at 2mm, 77 (17%) at 3mm, and 136 (33%) at 7mm. ‘Range’ demonstrated a peak in specificity at 3mm (0.975), with relatively stable sensitivity throughout (maximum 0.576 at 2mm, minimum 0.475 at 4mm).

‘Target Temperature’: The implementation of the ‘Target Temperature’ resulted in VisiTag ‘shadow’ gaps increasing from 77 sectors (17%) to 342 sectors (79%), with a consequent improvement in sensitivity from 0.489 to 0.928 at the cost of a much lower PPV (0.907 to 0.377, $p<0.001$).

Impedance Drop’: this binary filter also increased gaps from 77 sectors (17%) to 299 sectors (69%), improving sensitivity (from 0.489 to 0.885) at the cost of a lower PPV (0.907 to 0.411, $p<0.001$).

Predictive model

A binomial logistic regression was performed to ascertain the effects of the ‘Force’, ‘Time’, ‘Target Temperature’ and ‘Impedance Drop’ thresholds on the likelihood of detection of CMR LGE scar gap. ‘Percentage Time’ and ‘Range’ were excluded due to significant collinearity with default values, and complex distribution of non-ordinate values respectively. The logistic regression model was statistically significant, $\chi^2(4)=148$, $p<0.0001$. The model explained 41.7% (Nagelkerke R^2) of the variance in scar formation and correctly classified 82% of cases. Specificity was 94.9% and sensitivity 56.8% at a cut-off value of 0.5. Of the four predictor variables, only ‘Force’ and ‘Time’ were statistically significant (Table 4).

Discussion

This study was designed to quantify the value of VisiTag markers in the prediction of gaps in CMR-assessed ablation lesion sets following AF ablation, as a non-invasive marker of chronic scar formation, and to examine the impact of variations in thresholds of each parameter. The principal findings are as follows:

1. VisiTag settings vary widely between operators
2. At default settings, VisiTag ‘shadow’ gaps demonstrate an excellent specificity (97.5%) but poorer sensitivity (50.4%) in the prediction of CMR scar gaps
3. ‘Force’: Higher VisiTag thresholds (>10g) are associated with slightly higher NPV but lower specificity and poorer PPV: scar is frequently created at lower CF
4. ‘Target Temperature’ and ‘Impedance Drop’: the implementation of these filters at these settings (42°C and 10 Ω respectively) increases the NPV for gaps, but at the cost of higher false positive rate.

Contact force

There is evidence for the improvement in procedural outcomes with the use of contact force technologies. Leading on from early benchmark clinical studies (TOCCATA study (2) and EFFICAS I (3)), meta-analysis has demonstrated the benefit of operator feedback of real-time CF. Use of CF technology is associated with reduced ablation time, reduced total procedural time and perhaps a reduced risk of recurrence (5, 22), but the findings have not been reproduced universally in carefully designed randomised studies (23, 24).

However, the target CF for creation of permanent, transmural lesions in the atrium remains unclear. The EFFICAS I study was the first to propose firm recommendations, suggesting that a target CF of >20g and FTI >400gs was associated with a reduced risk of electrical reconnection at 3 months on invasive testing. These targets were used in the subsequent EFFICAS II study, which reported a consequentially improved durability of PV isolation at three months (98%, compared to 81% in EFFICAS I) (25). Most other studies, though, have not stipulated a target CF, in the context of increased risk of complications with high CF (4). SMART-AF showed that clinical outcome was improved when ≥80% of ablation lesions were performed within 'user-defined' target ranges (overall average CF 17.9±9.4g), whilst TOCCASTAR noted that ablation effectiveness improved from 58% to 76% with the use of 'optimal CF', defined as ≥90% of lesions created with CF ≥10g. Such findings are difficult to implement clinically, and may suggest that consistent catheter control, rather than CF alone, is also a strong determinant of effective and contiguous lesion formation.

Further studies have suggested that more conservative CF levels may be safer and equally efficacious. Pre-clinical work by Williams et al (10) found no difference in chronic atrial lesion formation using high CF (22.6±11.4g) versus low CF (7.8±4.0g), validated on LGE imaging, chronic voltage mapping and histology. In patients, Kimura et al (26) found no improvement in ablation, in terms of residual acute electrical connection, for CFs between 10-15g versus ≥15g. Furthermore, SMART-AF found an increased rate of procedural major adverse events with CF ≥ 14g, and Chelu and colleagues recently demonstrated increased oesophageal enhancement with CF >12g (27).

In this context, the findings of this study are highly relevant. The fixing of 'Time', 'Range' and 'Percentage Time' thresholds controls for variation in catheter stability on assessment of the impact of CF. Here, the specificity of gaps between VisiTags for prediction of CMR scar gaps was unchanged between 2 and 8g, but then fell markedly at higher CF, suggesting that chronic scar was frequently formed at lower CF. However, the sensitivity and negative predictive value of VisiTag gaps did continue to improve marginally with increasing CF ≥10g. The selection of a CF threshold is, unsurprisingly, a trade-off between confidence in efficacy and safety. However, this study quantifies the diminishing benefit of increasing thresholds above 12g.

Ablation time

Increased total ablation time and FTI have been shown to be associated with improved ablation efficacy (3, 28), and increased chronic scar formation on CMR imaging (8), but no clinical studies have clearly dissociated the effect of time from force. There is a suggestion that the effect of RF energy on chronic lesion formation may begin to plateau above FTI values of 500gs (28) or total 20seconds of effective ablation (9). In this study there was improved sensitivity for lesion gaps when increasing time thresholds up to 30 seconds, with no significant plateau of specificity, in contrast to 'Force' thresholds. The FTI was not formally assessed on account of the complex interplay with the 'Range' parameter (see Supplementary Figure 8). However, at the highest 'Force' and 'Time' thresholds (20g or 30sec), minimum FTIs were approximately 200gs and 300gs respectively, and FTI exceeded 1000gs at <1% of VisiTags at default settings.

Other parameters

Alteration of 'Range' and 'Percentage Time' thresholds demonstrated only a minor impact upon VisiTag performance. 'Range' reflects the distance the catheter is allowed to travel before ablation indices are allocated to a separate VisiTag marker. The decrease in number of markers at higher 'Range' thresholds reflects the increased area that the marker represents, despite the increased leniency of the marker threshold. The peak number of markers at 3mm (see Online Supplement) suggests that this may be a suitable setting to capture both catheter stability and ablation location.

'Percentage Time' reflects a rolling average of the amount of time that the CF has been greater than the minimum stipulated force, and as such it would be anticipated to be a marker of catheter stability. However, on assessment of the data in this study the 'Percentage Time' was found to be >80% for the vast majority of lesions, and therefore it has proved an ineffective filter at default 'Force' 8g. At higher target CF it may become a more discriminant index of catheter stability.

‘Target Temperature’ and ‘Impedance Drop’ filters are used by few operators (11, 12), but they clearly improve discrimination in terms of NPV. It may be most appropriate that the filters are not used during ablation, but only for retrospective review of ablation parameters. In view of the limited implementation of the filters, only a single filter setting was assessed. They may warrant further assessment in the future (see supplementary Figures 9 and 10).

CMR imaging assessment of chronic scar

LGE CMR techniques have been shown to be a valid and reproducible (13) assessment of chronic ablation scar injury, associated with clinical outcome measures (14–16, 29–31). There is also corroborative evidence that the qualitative correlation between ablation indices and CMR-derived scar is strong. Andreu et al (32) demonstrated a strong relationship between minimum CF and visual assessment of location of gaps in CMR-derived scar. At a CF of >12g there was >94% specificity in prediction of an uninterrupted ablation line in one of the 18 PV segments, but there was no control for the impact of time or catheter stability.

Limitations

The use of the LGE as the gold standard for scar formation is a technique that has been shown to be specific to the presence of scar, but with lower sensitivity (16, 33). Despite the implementation of best-practice imaging (18) and interrogation techniques, LGE may have missed scar where it was in fact present, and this would imply that lower thresholds than those identified may be effective. There is also the possibility of mis registration of the CMR to EAM shell: the impact of the registration was minimized through the use of a segment-by-segment analysis, but there remains the possibility of ascribing ablation or CMR enhancement to the wrong segment at the segment margins. Furthermore, as per common clinical practice, the VisiTag size for analysis was not varied with the parameters, but it is highly likely that the true lesion size increases on average with more stringent VisiTag parameters. All ablation procedures were clinical ablations, aiming for a uniform target force of >5g for at least 15seconds, and therefore variability in ablation parameters was relatively restricted. Finally, VisiTag annotation does not take into account power delivery: this is certainly another important factor in lesion formation and may have varied more significantly using temperature-controlled ablation as in this study. Newer objective lesion annotation indices integrate this parameter (34), and further evaluation of outcome is required.

Conclusion

Markers (VisiTags) calculated on objective assessment of ablation parameters are predictive of chronic CMR enhancement on sector-by-sector assessment. Mature atrial ablation scar formation, as assessed using CMR LGE techniques, increases in a non-linear fashion with increased contact force, and in a linear fashion with increased ablation time. The relationship with stability indices, 'Percentage Time' and 'Range' is more complex, with 'Percentage Time' having minimal impact on predictive value. This study provides a detailed clinical assessment of the impact of objective ablation parameter thresholds on CMR-derived atrial scar. It quantifies the relationship between sensitivity and specificity at each threshold, assisting informed clinician selection of threshold values.

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Figure Legends

Figure 1. VisiTag locations with variation of 'Force' (grams). Colouring of tags is according to FTI (force time interval) in gram.seconds. LIPV: left inferior pulmonary vein (PV), RIPV: right inferior PV, RSPV: right superior PV, LIPV: left inferior PV.

Figure 2. Example of the impact of 'Force' threshold alteration. CMR signal intensity (blue-red shell, scar in red) with VisiTag locations overlaid in grey 'shadow' at varying thresholds (2-20grams). Note over-estimation of lesion formation compared to chronic scar at low threshold (low sensitivity for gaps), and underestimation of scar formation (low specificity for gaps) at high thresholds.

Figure 3. (Top) Regional distribution of gaps in CMR LGE scar across all subjects. (Middle and lower) Highest thresholds that could be applied in each sector without gaps being demonstrated within VisiTag 'shadows' for 'Force' (middle- in grams) and 'Time' (lower- in seconds). Values are median with interquartile range (IQR). For sector 9 (inter-ostial) – CMR gaps (upper) is percentage of all subjects, regardless of whether ablation was performed, but in middle and lower plots, values reflect only subjects in whom inter-ostial ablation was performed. LS: left superior pulmonary vein, LI: left inferior, RS: right superior, RI: right inferior.

Figure 4. Top panel: Frequency histogram demonstrating false negative (FN), true negative (TN,) true positive (TP), and false positive (FP) frequencies for prediction of CMR scar gaps by gaps in VisiTag 'shadow' at default settings (see text). Rows 2 and 3: Receiver operator characteristic (ROC) curves for prediction of CMR scar gaps by VisiTag 'shadow' gaps, over multiple thresholds. Bottom row: Frequency histograms demonstrating prediction of CMR scar gaps by gaps in VisiTag 'shadow' with activation of 'Imp' or 'Temp' filters. AUC: area under curve.

Figure 5. Negative predictive value (NPV) and positive predictive value (PPV) of a gap in VisiTag 'shadow' within each sector predicting a gap in continuous scar on CMR LGE.

Tables

	Units	Full Description	Number of settings	Setting values	Default value
"Force"	Grams (g)	Force over Time-Minimum Force	10	2-4-6-8-10-12- 14- 18-20	8
"Time"	Seconds (s)	Stability Minimum Time	6	5-10-15-20-25-30	10
"Percentage time"	%	Force over Time-Time (%)	6	30-40-50-60-70-80	50
"Range"	mm	Stability Maximum Range	6	2-3-4-5-6-7	3
"Imp"	Ohms (Ω)	Impedance Drop	2	on (10Ω), off	Off
"Temp"	Celsius (°C)	Target Temperature	2	on (42°C), off	Off

Table 1. VisiTag parameters and settings used in the data exports.

	Gap detected (Gap in CMR Scar within sector)	**No gap detected** (Continuous CMR-scar within sector)	
Gap predicted (Gap in VisiTag 'shadow' within sector)	True Positive (TP)	False Positive (FP)	**Positive Predictive Value** *(nTP)/(nVisiTag gap)*
No gap predicted (Continuous VisiTag 'shadow' within sector)	False Negative (FN)	True Negative (TN)	**Negative Predictive Value** *(nTN)/(nVisiTag n gap)*
	Sensitivity *(nTP)/(nCMRscar gap)*	**Specificity** *(nTN)/(nCMRscar no gap)*	**Accuracy** *(nTP+nTN)/(nAll Sectors)*

Table 2. Methods for determination of key indices of VisiTag performance. n(group) indicates the number of points within each subgroup.

	All Subjects (n=24)
Male	18 (75%)
Paroxysmal AF	11 (61%)
CHA_2DS_2VASC Score	1 (IQR 0-2)
AF duration (years)	3.0 (IQR 1.75-5.5)
Age (years)	62 ±11
Weight (kg)	88 ±20
Height (cm)	175 ±8
BMI (kg/m^2)	28.9±6.7
Max LA volume pre-ablation (ml)	130±42
Max LA volume at post-ablation scan (ml)	124±40

Table 3. Summary of baseline demographics and scan characteristics. LA volume assessed using CMR. AF: atrial fibrillation, BMI: body mass index, LA: left atrium

	Odds Ratio	**95% CI**		**Significance**
		Lower	Upper	
'Force' (per gram)	1.14	1.075	1.208	<0.0001
'Time' (per second)	1.054	1.016	1.093	0.005
'Target Temperature'	0.973	0.443	2.137	0.946
'Impedance Drop'	0.659	0.341	1.273	0.214
Constant	0.215			0.009

Table 4. Variables in equation: binomial logistic regression. CI: confidence interval.